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THE APPLICATION OF CALCIUM CARBIDE IN THE SYNTHESIS OF D-LABELED PYRAZOLES

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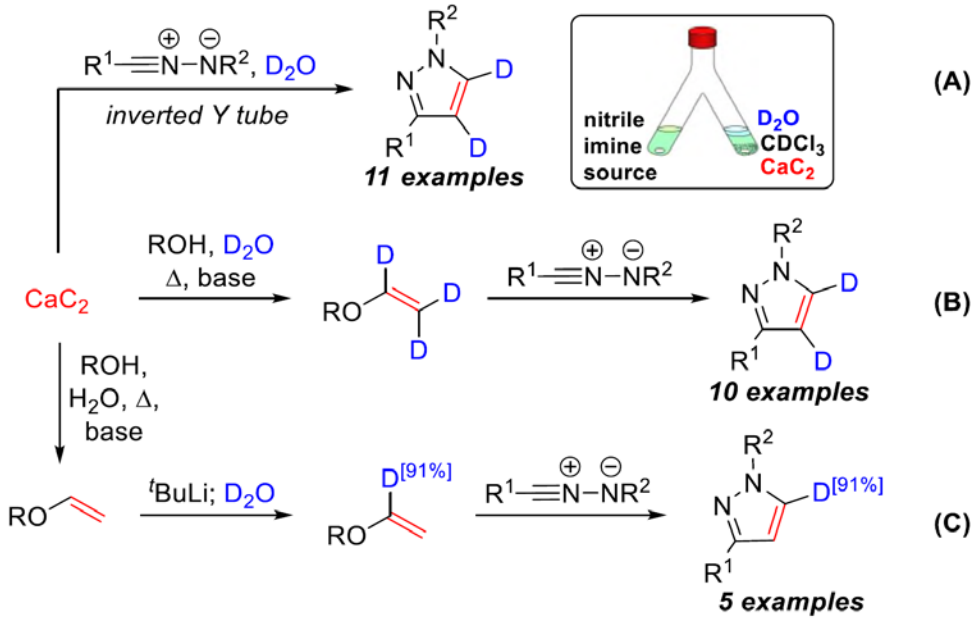
Abstract. Significant difference in C-D and C-H bonds strengths is extensively used in various chemical and biomedical applications. The comparison of the C–H bond and C–D bond reactivity was often applied in the studies of reaction mechanisms [1]; the substitution of hydrogen by deuterium was also applied to alter the reactions selectivity [2] and for the management of pharmacokinetic profile of drugs [3]. The latter advances in this field (for example, the actual approval of the first deuterated drug, deutetrabenazine [4]) made the synthesis of new deuterated substances a demanded goal for organic and pharmaceutical chemistry.

The synthesis of D-labeled pyrazoles, in particular, the ones with regioselectively located deuterium, is of great interest. We proposed a synthetic approaches to 4,5-dideuteropyrazoles and regioselectively labeled 5-deuteropyrazoles. The application of CaC_2-D_2O mixture as a source of D_2-acetylene in the reaction with *in situ* generated nitrile imines led to a variety of 1,3-disubstituted D_2-pyrazoles in up to quantitative yields (part A). The reaction was performed in two-vessel reactor, demonstrated in the part A [5].

The use of CaC_2-derived vinyl ethers and D_3-vinyl ethers is another opportunity for the synthesis of pyrazoles. The interaction of D_3-vinyl ethers with the nitrile imine source led to a range of D_2-pyrazoles in 66–99% yields (part B) [6]. 1-Deuterovinyl ether led to 5-deuteropyrazoles (part C) in excellent yields and 100% regioselectivity [6].



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